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1907

On Aldol, Pentaerythrose and the Action of Copper Acetate on the Hexoses

A DISSERTATION

SUBMITTED TO THE FACULTY OF THE OGDEN GRADUATE SCHOOL OF SCIENCE, IN CANDIDACY FOR THE DEGREE OF DOCTOR OF PHILOSOPHY

DEPARTMENT OF CHEMISTRY

BY

ANDREW FRIDLEY McLEOD

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On Aldol, Pentaerythrose and the Action of Copper Acetate on the Hexoses.

All the condensation reactions shown by aldehydes in the presence of alkalies have been classified by Nef[1] under the head of olefine and alkylidene condensations.

It is now possible, in the light of Nef's work on aldehydes, alcohols, etc., during the past 12 years[2] and because of some observations of my own on acetaldehyde which were made at Dr. Nef's suggestion and under his guidance, to formulate these reactions more precisely. An aqueous solution of an aldehyde contains the following substances in dynamic equilibrium:

$$\underset{\text{Aldehyde.}}{RHC:O} + H_2O \rightleftarrows \underset{\text{Alkylidene dihydroxide.}}{RHC(OH)_2} \rightleftarrows \underset{\text{Hydroxyalkylidene.}}{RCOH} + H_2O.$$

$$[R = C_nH_{2n+1},\ C_6H_5 \text{ or } H.]$$

Now it is well known that an aldehyde, in aqueous solution, never goes over into its condensation products at temperatures between 20° and 100°; polymerization of the active aldehyde molecules,

$$3RHC(OH)_2 \rightleftarrows (RHC(OH)_2)_3,$$

on the other hand, may often take place spontaneously.

When we treat an aldehyde with an aqueous solution containing an alkali or an alkaline salt, *e. g.*, caustic or mild alkalies, potassium cyanide, sodium or potassium formate or acetate, etc., condensation often takes place at once in the cold even in the presence of a marvelously small amount of the reagents named. What is the function of the alkali in these cases and how may its concentration affect the end result? The aldehydes in the form of their hydrates are $RHC(OH)_2$, the alkylidene dihydroxides are really diatomic alcohols; they must, there-

[1] Ann. Chem. (Liebig), **298**, 219-223.

[2] *Ibid.*, **298**, 202-374; **309**, 126-189; **310**, 316-335; **318**, 1-57, 137-230; **335**, 191-333.

fore, possess, like all alcohols, weak acid properties and be capable of salt formation;[1] and the exhaustive experiments of Nef on the monatomic as well as on the polyatomic alcohols have shown conclusively that the salts of all primary and secondary alcohols are relatively much more dissociated into alkylidene,

$$RR'CHOM \rightleftharpoons RR'C< + HOM,$$

than the corresponding free alcohols. It is, therefore, self evident that an aldehyde in the presence of an alkaline salt, or even of powdered calcium carbonate at 100°,[2] must be *relatively more* dissociated into hydroxyalkylidene,

$$R(HO)CHOM \rightleftharpoons R(HO)C< + HOM.$$

As soon as the concentration of the hydroxyalkylidene reaches a certain definite limit, a condensation reaction, or a decomposition of the water present by the hydroxyalkylidene must take place. Often both reactions occur simultaneously.

Thus, according to unpublished observations of Nef, when 4 liters of 1 per cent aqueous formaldehyde are treated, in the cold, with 24 grams of powdered quicklime, 80 per cent of the reaction proceeds slowly according to

$$\text{(I)}\quad CH_2O + (HO)CH< + 2HO{-}H \rightarrow HOCH(OH)_2 + 2H{-} + CH_2{-}O \rightarrow \begin{matrix} & & H & OH \\ & & C & \\ & & \| & \\ & & O & \end{matrix} + H_2O + CH_3OH,$$

and only 20 per cent according to

$$\text{II.}\quad 6HOCH< \rightarrow 3 \begin{matrix} HOCH \\ \vdots \\ HOCH \end{matrix} \rightarrow 3HOCH_2CH:O \rightarrow C_6H_{12}O_6.$$

If, on the other hand, small amounts of lead hydroxide,[3] or powdered calcium carbonate[4] be used in place of lime, then re-

[1] Nef: Ann. Chem. (Liebig), **318**, 138–187; **335**, 312. Cf. Euler: Ber. d. chem. Ges., **39**, 36–45.

[2] Euler: Ber. d. chem. Ges., **39**, 45.

[3] Lobry de Bruyn and Ekenstein: Rec. Trav. Chim., **18**, 309.

[4] Euler: Ber. d. chem. Ges., **39**, 45.

action II., *i. e.*, sugar formation, is the chief reaction. The remarkable difference in the result is obviously simply due to the fact that the concentration of hydroxymethylene, present in Lobry de Bruyn's and in Euler's experiments, is *far smaller* than when lime, or some other caustic alkali is used; consequently polymerization of 2 hydroxymethylene molecules to dihydroxyethylene which then goes over spontaneously into glycolyl aldehyde, etc., is the chief reaction in the former case. Similarly 2 molecules of hydroxyphenylmethylene, C_6H_5COH, formed from benzylidenedihydroxide by dissociation, polymerize[1] to dihydroxystilbene, $\begin{matrix} C_6H_5COH \\ \vdots\vdots \\ C_6H_5COH \end{matrix}$, which then spontaneously transforms itself, probably, without an intermediate addition of water, into benzoin, $C_6H_5C : OCH(OH)C_6H_5$. In the case of benzaldehyde the benzoin condensation (*i. e.*, reaction II.) is possible only by using small amounts of potassium cyanide, which here obviously serves a double purpose, first in increasing the amount of methylene dissociation and second in uniting temporarily with the hydroxyphenylmethylene to form an easily dissociable double salt, $C_6H_5(HO)C:CNK$, analogous to the double cyanides and fulminates.[2] When, on the other hand, benzaldehyde is treated with cold, concentrated, aqueous potassium hydroxide, molecular amounts of benzyl alcohol and benzoic acid are formed according to reaction I. It should be *especially emphasized* that only *tertiary* aldehydes, such as benzaldehyde, trimethylacetaldehyde, $(CH_3)_3 : CCH:O$, etc., *i. e.*, those which contain the aldehyde group bound to a carbon atom which is free from hydrogen can undergo the benzoin condensation—which is simply due to a polymerization of two hydroxyalkylidene molecules,

$$2RCOH \rightleftharpoons \begin{matrix} RCOH \\ \vdots\vdots \\ RCOH \end{matrix},$$

etc. The conversion of formaldehyde into glycollic aldehyde

[1] Nef: Ann. Chem. (Liebig), **298**, 312.

[2] Nef: *Ibid.*, **280**, 334-338; **298**, 313. Cf. Goldthwaite: Am. Chem. Jour., **30**, 466, foot-note.

must, however, also be considered as a benzoin condensation. Why is it that the ordinary aliphatic aldehydes do not undergo an analogous benzoin condensation on treatment with alkaline reagents? The reason for the well-known difference in behavior is easily understood on the basis of the following considerations which have been presented for some years past by Dr. Nef in his lectures on organic chemistry, and which are simply an application of his ideas on the laws of condensation presented in a paper of his.[1] A primary or a secondary aldehyde, $RCH_2CH:O$ and $(RR')CHCH:O$, still contains on the carbon atom holding the CHO group one or more easily dissociable non-ionic hydrogen atoms.

When, therefore, the concentration of the hydroxyalkylidine molecules is in these cases increased by the addition of a mild or caustic alkali, or an alkaline salt, the following 2 entirely independent reactions may take place simultaneously or singly:

(I.) Decomposition of the water, or caustic alkali present by the hydroxyalkylidene according to

$$RR'CH{-}\underset{|}{CH}{-}\underset{|}{O} + RR'CH{-}\overset{\diagup\diagdown}{C}(OH) + 2H{-}OH \Longrightarrow RR'CHCH_2OH + RR'CHC(OH)_3.$$

Reaction I. is, therefore, common to all aldehydes, whether primary, secondary or tertiary; the Dumas-Stas reaction, whereby all aldehydes are converted quantitatively by potash-lime at 200°–250°, into hydrogen and the potassium salt of the corresponding fatty acid,

$$RCH:O + KOH \Longrightarrow RCOOK + H_2,$$

is obviously simply a special phase of reaction I.

(II.) The hydroxyalkylidene may transform itself, by intramolecular addition,[2]

$$RR'\overset{\diagup\diagdown}{CHCOH} \Longrightarrow RR'\underset{||}{CCHOH} \Longrightarrow RR'C:CH(OH),$$

into an olefine derivative, which then at once unites with the unchanged aldehyde present, according to

[1] Ann. Chem. (Liebig), **298**, 202-374.
[2] Nef: *Ibid.*, **318**, 1-57; **335**, 196-200.

$$RR'CCH(OH) + H{-}CRR'CHO \rightleftharpoons (RR')CHCH(OH)CRR'CH{:}O,$$

giving an aldol (olefine condensation). The aldols thus formed may then give in many cases, by further loss of water, olefine derivatives, *e. g.*, acetaldol goes over, in the presence of traces of alkali or acid, with remarkable ease, by loss of water, into crotonaldehyde, in 2 stages, see below. A polymerization of 2 hydroxyalkylidene molecules,

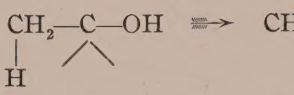
$$(RR')CHCOH,$$

to a benzoin-like body,

$$RR'CHC(OH){:}C(OH)CHRR' \rightleftharpoons RR'CHCOCH(OH)CHRR',$$

which is also possible from a theoretical standpoint in the case of primary and secondary aldehydes has, up to the present time, never been observed; such a transformation is, indeed, highly improbable because of the ease with which the intramolecular addition reaction II., just cited, must take place as soon as the concentration of the hydroxyalkylidene present is above a definite limit. It is, however, not impossible that in the future certain primary and secondary aldehydes may be found which, in addition to the ordinary aldol condensation, may also undergo a benzoin condensation.

In studying the action of caustic alkalies and alkaline carbonates on acetaldehyde I have, moreover, made the following important observation: When the concentration of alkali used is below a certain definite limit, which is 0.1 per cent in the case of sodium and calcium hydroxides, no appreciable condensation of the acetaldehyde to aldol or crotonaldehyde takes place, even after weeks of standing at ordinary temperatures. This is just what one would expect from the theory presented above, a certain definite amount of alkali is obviously necessary in order to increase the concentration of the hydroxyethylidene molecules in quantity sufficient to enable the transformation into vinyl alcohol,



to take place, and this is a condition *sine qua non* in Nef's theory of aldol condensation. Nef has shown, furthermore, that when freshly precipitated oxide of mercury is present the vinyl alcohol first set free by the addition of alkalies is prevented from uniting with unchanged aldehyde to give aldol because it unites *by preference* with the metallic oxide introduced into the system[1] to form an insoluble white salt, which readily gives back acetaldehyde on treatment with dilute acids.

Finally, it is well known from Lieben's experiments that when molecular mixtures of various aliphatic aldehydes are treated with alkalies, only one of the two theoretically possible mixed aldols is formed; thus acetaldehyde gives, with isobutyric aldehyde, only

(I.) $CH_3CH(OH)C(CH_3)_2CH : O$,

and not a trace of

(II.) $(CH_3)_2CHCH(OH)CH_2CH : O$.

This can only be due to the fact that acetaldehyde is converted into vinyl alcohol far more readily and with much smaller concentration of the alkali than is isobutyric aldehyde into the corresponding vinyl alcohol homologue, $(CH_3)_2 : CCH(OH)$; consequently, vinyl alcohol absorbs isobutyric aldehyde to give product I.

The fact that remarkably different minimal concentrations of alkali are required in the case of the various aldehydes in order that a transformation according to II., *i. e.*, a benzoin or aldol condensation may take place, is of the utmost importance in synthetic work. Thus it is clear that when aqueous mixtures of acetaldehyde and formaldehyde are treated with potassium or sodium hydroxides, taking care to keep the concentration of the alkali used below 0.1 per cent, no trace of aldol or crotonaldehyde can be formed; the formaldehyde, on the other hand, which is by far the most sensitive of all the aldehydes towards alkalies and is even condensed in the presence of calcium carbonate to

[1] Ann. Chem. (Liebig), **298**, 316-318,

hexoses, must contain, under the conditions named, a sufficiently large concentration of hydroxymethylene molecules to form at once with the acetaldehyde present a mixed aldol. Tollens[1] has, in fact, shown that one can obtain large amounts of pentaerythrite, $C(CH_2OH)_4$, from aqueous solutions of acetaldehyde and formaldehyde (4 mols.) in the presence of calcium hydroxide. It is evident, from Nef's work, that this reaction proceeds through the following 5 successive stages:

$3HOCH< + H—CH_2CHO \rightarrow$

Hydroxymethylene (*a*).

$HOCH_2CHHCHO + HOCH< \rightarrow$

Hydracrylic aldehyde (*b*).

$(HOCH_2)_2CHCHO + >CHOH \rightarrow (HOCH_2)_3CCHO$

$\beta\beta'$-Dihydroxyisobutyric aldehyde (*c*). Pentaerythrose (*d*).

$(CH_2OH)_3 : CCHO + >CHOH + 2H—OH \rightarrow$

$(HO)_2CHOH + (CH_2OH)_3 : CCH_2OH.$

Pentaerythrite (*e*).

I have consequently taken up, at Dr. Nef's wish, a renewed study of the action of alkalies on mixtures of acetaldehyde and formaldehyde with the object of proving, by experiment, that the reaction takes place through the stages indicated; it was *a priori* improbable that an intermediate formation of hydracrylic aldehyde (*b*), or even of $\beta\beta'$-dihydroxyisobutyric aldehyde (*c*) could be proved by direct means, since the non-ionic α-hydrogen atoms still left bound to the carbon atom containing the CH:O group in these intermediate products must be *relatively* far more dissociated from carbon than the corresponding ones in acetaldehyde; consequently these substances must, in the main, be at once absorbed by more hydroxymethylene to give pentaerythrose (*d*).

I succeeded, therefore, in obtaining large amounts of pentaerythrose in the reaction under discussion; and the indications point also to the presence of relatively large amounts of $\beta\beta'$-dihydroxyisobutyric aldehyde (*c*) in the crude material obtained. That the reaction proceeds through stage (*b*) was, furthermore,

[1] Ann. Chem. (Liebig), **265**, 316; **276**, 158.

definitely established because mixtures of hydracrylic aldehyde, which has recently been discovered by Nef, and of formaldehyde (2 mols.) give, when treated with traces of sodium hydroxide, an almost quantitative yield of crude pentaerythrose.

EXPERIMENTAL PART.

It is clear from a study of the literature on the subject that acetaldehyde, when treated with mild or caustic alkalies, or with concentrated sulphuric acid, is transformed successively into aldol, crotonaldehyde, oily volatile and non-volatile condensation products of crotonaldehyde and, finally, into aldehyde resin; the constitution, or even the homogeneous character of the 3 last-named products, has not yet been ascertained.

The following experiments with acetaldehyde prove that when the concentration of the mild or caustic alkali used is below a certain definite limit, no condensation of the acetaldehyde takes place even on 6 weeks' standing at ordinary temperatures; furthermore, the conditions under which the best yield of aldol and of crotonaldehyde can be obtained from acetaldehyde were thoroughly investigated. It was definitely established that aldol, as well as crotonaldehyde, never gives back a trace of acetaldehyde on treatment with water, with very dilute alkalies, or with acids in sealed tubes at 100°. Aldol goes over, under these conditions with the greatest ease, into crotonaldehyde, which is, in turn, converted into insoluble, yellow, volatile and non-volatile oils and, finally, into aldehyde resin.

Manufacture of Acetaldehyde and Its Behavior towards Dilute Alkalies.

Since preparations of acetaldehyde invariably contain a greater or less proportion of paraldehyde, all the acetaldehyde used in my experiments was prepared from paraldehyde by dissociation. A few drops of concentrated sulphuric acid have been usually used for this purpose, but there is always considerable loss through charring by this process. The following method is thoroughly reliable and always gives at least a 90 per cent yield. Paraldehyde, 212.2 grams, and 20 per cent sulphuric acid, 10 cc., are mixed and heated in a flask provided

with a Glinsky apparatus. The temperature of the surrounding bath is kept at 85°–95°, whereupon acetaldehyde rapidly distils over; on redistillation, 190.4 grams of aldehyde, b. p. 21°–27°, were regularly obtained. Ten grams of aldehyde were dissolved in the cold in 10 cc. of saturated lime water, proved by titration with standard acid to contain 0.01617 gram of calcium hydroxide; the mixture was then allowed to stand at room temperature for 6 weeks. On heating the alkaline solution on a boiling water-bath and subsequently drying the distillate with calcium chloride, 8.4 cc. of aldehyde, b. p. 21°–30°, were recovered unchanged. This is 67.2 per cent of the amount originally taken.

A second experiment, in which 10 grams of aldehyde and 10 cc. of 0.1 per cent sodium hydroxide, containing, as determined by titration with standard acid, 0.01154 gram of sodium hydroxide, were used, gave the following result: After standing for 21 days at room temperature no trace of coloration or of formation of insoluble aldehyde resin could be observed. The alkaline solution was now heated on a boiling water-bath to drive off the unchanged aldehyde, proceeding as in the first experiment. Seven and eight-tenths cc. of aldehyde, b. p. 21°–30°, were recovered. Furthermore, titration of the aqueous alkaline solution, left after distilling off the aldehyde, with standard acid proved that 0.0112 gram of sodium hydroxide was still present, only 0.3 milligram, therefore, had been used up. These experiments prove that when the concentration of the calcium or sodium hydroxide solutions is 0.1 per cent no condensation or only exceedingly slow condensation of acetaldehyde takes place. It is very probable that 0.2 per cent sodium or potassium carbonate solutions will have no condensation effect on aldehyde. I expect, moreover, to continue experiments in this direction at once, in the autumn, including also a study of the action of such substances as potassium cyanide, sodium and potassium acetate, etc.

Manufacture of Aldol and of Crotonaldehyde, and Behavior of These Substances towards Water, Dilute Alkalies and Acids, Etc.

The only 2 satisfactory methods of preparing aldol in quan-

tity are those of Halpern[1] and of Orndorff and Newbury[2] from acetaldehyde and small amounts of powdered potassium carbonate, or 10 per cent aqueous potassium carbonate, respectively. In both cases the yield of pure distilled aldol obtained was never over 50 per cent of that demanded by theory. I have always obtained a large and practically constant yield, 60 per cent, of aldol by the following method, which is essentially that of Orndorff and Newbury.

A solution of 47 grams of aldehyde in 20 grams of water was treated, in the cold, with 2 grams of potassium carbonate, dissolved in the smallest possible amount of water. The temperature was kept below 10° for the first half hour and the mixture was then left standing, at ordinary temperatures, for 18 hours. The aldol was removed from the aqueous solution by extracting 3 times with ether. After drying with calcium chloride, and removing the last traces of ether by heating in a flask, up to 80° (20 mm.), 41 grams of crude, yellowish aldol were obtained. This gave, on distillation, 28.3 grams of the pure product boiling at 79° (20 mm.) and only 5.1 grams of higher boiling oil remained in the distilling flask. Considerable loss, 15–20 per cent, must, therefore, have occurred through volatilization. Two further experiments, carried out in practically the same manner, and with the same amount of material, gave, after 1 distillation, 48–50 per cent of pure aldol and 20–35 per cent of higher boiling oils.

Another experiment with 20 grams of aldehyde, 8 grams of water and 1 gram of potassium carbonate gave, after 18 hours' standing, by acidifying with the calculated amount of hydrochloric acid and then heating on a boiling water-bath, 3 cc. of aldehyde, boiling at 21°–35°; this proves that about 12 per cent of the aldehyde is left unchanged in the process used. Nevertheless, it is not advisable to allow the alkaline solutions to stand longer than 18 hours, to insure complete transformation of the aldehyde, because aldol itself is rapidly acted upon under the conditions employed, as was also proved by special experiments. Thus it was observed that when the alkaline solu-

[1] Monats. Chem., **13**, 517.
[2] *Ibid.*, **22**, 59.

tion stood longer, 48 hours for example, instead of 18, only 20–30 per cent, or even less, of pure aldol was obtained and the amount of non-volatile and higher-boiling yellowish oil was correspondingly increased. Special experiments have also shown that it is impossible to obtain aldol in appreciable quantity from aldehyde either by means of traces of powdered potassium hydroxide or by using aqueous solutions of this substance in concentration varying from 0.1 per cent to 2 per cent.

In order, finally, to obtain crotonaldehyde in quantity for investigation it was found, after repeated trial of various methods given in the literature, that the following process gives by far the best yield: Crude aldol, made from aldehyde and 10 per cent potassium carbonate, as stated above, is mixed with 0.5 of its weight of powdered potassium bisulphate and heated rapidly first at 120°–130° and finally in a bath at 180°–200.° The distillate, after separating from small amounts of water and drying with calcium chloride, boils at once at 98°–106°. The yield was found to be regularly 70–73 per cent of that demanded by theory.

My experience with Lieben's method[1] for making crotonaldehyde was as follows: A mixture of 15 cc. of acetaldehyde and 5 cc. of 28 per cent sodium acetate was heated for 10 hours, in a sealed tube, at 100°. On working up by heating first in a bath at 100° and then at 120°–130°, etc., 9 cc. of acetaldehyde, 2.4 cc. of crotonaldehyde, boiling at 98°–106° and 1.2 grams of yellow, mobile oil, boiling at 90°–120° (24 mm.) were obtained. Similar mixtures of aldehyde and sodium acetate, when heated longer at 100°, *e. g.*, for 36 hours, gave only small amounts of unchanged aldehyde and of crotonaldehyde. The main product was an insoluble, reddish, mobile oil which, on fractionation (20 mm.), boils in part at 90°–120° and leaves much non-volatile, viscous, red gum—obviously condensation or polymerization products of crotonaldehyde. Finally, Orndorff and Newbury's method of making crotonaldehyde,[2] by direct heating of aldol under ordinary pressures, gave, under the most

[1] Monats. Chem., **13**, 519.

[2] *Ibid.*, **13**, 517.

favorable conditions, only a 37.5 per cent yield of the product. Thus 13.5 grams of aldol, boiling at 79° (20 mm.), when heated in a flask connected with a Glinsky apparatus, a condenser, and well-cooled receiver, gave, finally, after heating in a bath from 190°–220°, 0.4 gram of aldehyde, boiling at 21°–30°, 4 grams of crotonaldehyde, boiling at 102°–106°, and 4 grams of much higher boiling yellow oil remained in the distilling flask. Furthermore, 11 grams of aldol, heated for 6 hours in a sealed tube at 180°–200°, gave an entirely similar result. An exceedingly good method for making crotonaldehyde is simply to heat aldol with 12 parts of water for 14 hours, in a sealed tube, at 100°; a 73 per cent yield is regularly obtained. No trace of aldehyde, but small amounts of yellow crotonaldehyde condensation products are also formed in this case. The separation of crotonaldehyde from water involves on difficulty, as on distillation of an aqueous solution the aldehyde comes over entirely with small amounts of water in the first portion of the distillate. The first fraction is, therefore, simply redistilled, or is often freed at once from small amounts of water by drying with calcium chloride, etc.

A solution of 6.4 grams of crotonaldehyde, b. p. 103°–104°, in 70 cc. of water, was heated in a sealed tube, at 100°, for 43 hours, with the following result: Three cc. of dry crotonaldehyde, boiling at 98°–103°, were recovered unchanged. On extracting the aqueous solution with ether, etc., only 0.5 gram of yellowish oil was obtained, one-half of which boiled from 84°–86° (29 mm.) and the remainder was non-volatile. It is possible that the small amount of volatile oil obtained was aldol but, unfortunately, we have no means of sharply identifying aldol by conversion into a crystalline derivative. In any case, the results obtained show that the behavior of aldol and crotonaldehyde towards water is in marked contrast to that of the lower homologues, hydracrylic aldehyde and acrolein.[1]

The following experiment made with crotonaldehyde and 0.1 per cent sodium hydroxide proves that it is slowly converted, at ordinary temperatures, into high-boiling and non-volatile red oils. Since acetaldehyde remains practically un-

[1] Ann. Chem. (Liebig), **335**, 219.

changed on similar treatment and aldol is converted very rapidly under these conditions, first into crotonaldehyde, etc., it is obviously impossible, by means of caustic alkalies, to convert aldehyde either into aldol or crotonaldehyde, as was also shown by special experiments described above.

In the first place it was proved that a mixture of 3.5 grams of crotonaldehyde and 3.5 grams of 0.1 per cent sodium hydroxide, when distilled directly, give back 2.7 grams of dry crotonaldehyde boiling at 98°–106°; in addition, 0.3 gram of non-volatile, insoluble, red oil was obtained.

Five and three-tenths cc. of crotonaldehyde were now dissolved in 30 cc. of cold 0.1 per cent sodium hydroxide and the mixture was then allowed to stand in a closed vessel for 14 days at ordinary temperatures. On distillation 2.2 cc. of unchanged crotonaldehyde, which is 42 per cent of the amount taken, were recovered; in addition 0.3 gram of thick red oil, boiling at 90°–120° (30 mm.), and 1.3 grams of brown, non-volatile resin were obtained from the alkaline solution by extraction with ether, etc.

On mixing equal volumes of aldol and 1 per cent sodium hydroxide in the cold, a noticeable rise of temperature is observed; the solution turns yellow, the odor of crotonaldehyde is very perceptible and soon an insoluble, yellowish oil separates out which gradually sinks and is transformed into a thick red oil. This oil, which is insoluble in water and freely soluble in ether, remains non-volatile when heated in a bath at 300° (20 mm.). Crotonaldehyde, on similar treatment, gives, apparently, the same red oil, which is obviously an intermediate product in the transformation of aldehyde, aldol, crotonaldehyde, etc., by caustic alkalies or concentrated sulphuric acid into aldehyde resin. The following experiments with aldol also show how readily this substance goes over into crotonaldehyde. A mixture of 6.4 grams of aldol, 14 cc. of water and 2 cc. of 0.1 per cent sodium hydroxide gave, after heating in a sealed tube at 100°, for 12 hours, no trace of acetaldehyde but 3.5 cc. of crotonaldehyde, or 71 per cent of the theory, and a total of 1.5 grams of high-boiling as well as non-volatile red oils.

Thirteen and three-tenths grams of aldol, b. p. 79° (20 mm.), and 50 cc. of water containing 1 gram of crystallized sodium acetate were heated in a sealed tube, for 20 hours, at 100°; no trace of acetaldehyde was formed, but 2.6 cc. of crotonaldehyde, boiling at 98°–106°, were obtained. The alkaline solution gave, on extracting with ether, etc., 5.8 grams of reddish oil which, on distillation (30 mm.), decomposed to a large extent, giving 1 cc. of yellowish, mobile oil, boiling at 100°–150° and leaving 1.6 grams of non-volatile red gum in the distilling flask.

A similar experiment, in which 13.9 grams of crotonaldehyde and 5 cc. of 28 per cent sodium acetate solution were heated in a sealed tube for 20 hours, at 100°, gave no trace of acetaldehyde but 6.4 cc. of unchanged crotonaldehyde and 4 grams of non-volatile reddish gum.

Six and five-tenths grams of aldol were dissolved, in the cold, in 70 cc. of water containing 0.5 gram of potassium carbonate. The solution became yellow and smelt strongly of crotonaldehyde. On working up in the usual manner, after 2 days' standing at ordinary temperatures, only a very small amount of crotonaldehyde and no trace of acetaldehyde was formed. The main product was a reddish, non-volatile gum, insoluble in water—obviously a condensation or polymerization product of crotonaldehyde.

A solution of 9.7 grams of aldol in 10 cc. of 1 per cent sulphuric acid was heated for 5 hours in a sealed tube, at 100°; 5.3 grams of thick brown oil had separated from the aqueous layer and was drawn off and distilled; 2 cc. of moist crotonaldehyde, boiling at 98°–106°, were obtained, but the main portion was a mixture of high-boiling as well as non-volatile red oils.

Similarly, 4 grams of aldol dissolved in 12 cc. of water containing 3 drops of 20 per cent sulphuric acid gave, after heating for 10 hours at 100°, in a sealed tube, no trace of aldehyde, 1.5 cc. of crotonaldehyde, 48 per cent of the theory, and a total of 1 gram of high-boiling and non-volatile reddish gum.

It is evident from the work of Nef that the function of the small amount of alkali or of sulphuric acid used in the experi-

ments described above is to form temporarily with the aldol a salt,

$$CH_3CH(OM)CH_2CHO,$$

or an ester,

$$CH_3CH(OSO_2OH)CH_2CHO,$$

which, being *relatively more dissociated* into the alkylidene derivative,

$$CH_3C< \quad \text{and} \quad HOM \quad \text{or} \quad H_2SO_4$$
$$O : CHCH_2$$

than the mother substance, enables the intramolecular transformation of the methylene derivative,

$$CH_3C<,$$
$$O : CH—CH—H$$

into crotonaldehyde

$$CH_3CH : CHCHO,$$

to take place *more rapidly* because of increased concentration.

On the Behavior of Acrolein and of Hydracrylic Aldehyde towards Alkalies.

A thorough investigation of the action of traces of mild and caustic alkalies on acrolein and on hydracrylic aldehyde was extremely desirable[1] and I therefore took up this study under Dr. Nef's guidance. The statement of Nef that these compounds are split under the conditions just named into crotonaldehyde, etc., was found to be incorrect. I have observed that all alkalies, both mild and caustic, when added in traces to a cold aqueous solution of acrolein invariably transform the substance quantitatively, and with marked evolution of heat, into an insoluble, amorphous polymer, which is perfectly analogous to the one obtained by Nef with acrolein and barium hydroxide. These polymers are neutral to sodium carbonate, but dissolve easily in 10 per cent sodium hydroxide and, after digesting for a short time at 100° and adding the calculated

[1] Ann. Chem. (Liebig), **335**, 220.

amount of hydrogen chloride, an amorphous, very high-melting substance is deposited whose weight is about one-half that of the polymer originally taken. The same end result is obtained with hydracrylic aldehyde and sodium hydroxide, although in this case no insoluble acrolein polymer is first deposited from the alkaline solutions on standing in the cold. These results made it impracticable to proceed further with the investigation and I therefore simply converted the remainder of my acrolein into hydracrylic aldehyde, in order to prove that this substance gives pentaerythrose, etc., when treated, in aqueous solution, with 2 mols. of formaldehyde, in the presence of traces of caustic alkali. All the acrolein used in my work was made from commercial glycerin and traces of phosphoric acid, according to Nef's directions.[1] I have found, after many trials, with 1 to 10 grams of phosphoric acid, that it is best to use 3 grams of phosphoric acid, sp. gr. 1.73, for every 100 grams of glycerin taken and to heat the mixture at first for 2.5 hours in a bath kept at 220°–240°, and then for one-half longer at 260°–300°. The yield of pure acrolein was regularly 10 grams for every 100 grams of glycerin taken, and the operation can be carried out successfully and without appreciable frothing by using 500 grams of glycerin at one time.

On the Acrolein Polymers.—Twenty-three and five-tenths grams of acrolein, b. p. 52°–58°, were dissolved in 184 cc. of water and 0.1 gram of potassium carbonate dissolved in 2 grams of water was then added in the cold. Turbidity sets in immediately and soon a large amount of a white substance separates out as a voluminous solid. The odor of acrolein was practically all gone after 18 hours' standing, but to insure complete transformation the mixture was treated with 0.1 gram more of potassium carbonate and allowed to stand 24 hours longer. Thus 22.5 grams of a white, amorphous substance, obviously, from its properties, polymeric acrolein were obtained. The polymer is insoluble in hot water, ligroin, ether, carbon bisulphide, benzene, glacial acetic acid; it dissolves easily in warm 95 per cent alcohol. On warming with dilute acids or alkalies, as well as on direct heating up

[1] Ann. Chem. (Liebig), **335**, 221, foot-note.

to 100° and above, a strong odor of acrolein is at once noticed. My substance softened at 83° and decomposed, with gas evolution, at 94°–95°, whereas the perfectly analogous compound obtained by Nef[1] softens at 115° and decomposes at 128°–130°. It is quite possible that the polymers are space isomers, but as neither product could be obtained in the crystalline form the homogeneous nature of each is uncertain. Both dissolve, however, on warming in 10 per cent sodium hydroxide and give, apparently, the same end product.

In repeating the experiment with 18.2 grams of acrolein, dissolved in 56 grams of water, it was observed that by an addition of 1 gram of potassium carbonate, dissolved in 4 cc. of water, a sudden and marked rise of temperature took place and that the transformation into the polymeric acrolein was practically complete in 15 minutes; 15 grams of amorphous substance, softening at 81° and decomposing at 94°–95°, were thus obtained.

Thirteen and eight-tenths grams of the polymeric acrolein were now heated in a distilling flask and the temperature of the surrounding bath was finally raised to 190°–220°; much tar formation took place and the distillate, 4.2 grams, gave, on fractionation, 2 cc. of acrolein boiling at 52°–60°.

As already mentioned, these polymers, as well as acrolein and hydracrylic aldehyde, all give red solutions on warming with 10 per cent sodium hydroxide; no crotonaldehyde nor its condensation products can have been formed in these cases for the solutions remain clear and give no aldehyde resin on long boiling.

After heating for 12 hours at 100° and then neutralizing with the calculated amount of hydrogen chloride, a light brown, flocculent precipitate is obtained. The weight in all cases was found to be about one-half of that of the substance taken. This precipitate is likewise amorphous, insoluble in water and practically all organic solvents and does not melt when heated up to 180°. It is neutral to sodium carbonate but dissolves easily and without change in sodium hydroxide.

[1] *Loc. cit.*

Pentaerythrose, $(CH_2OH)_3 \vdots CCH:O$, from Mixtures of Formaldehyde and Acetaldehyde or Hydracrylic Aldehyde, Respectively.

A solution containing 15 grams of aldehyde, 354 cc. of water and 87.6 grams of 35 per cent formaldehyde (3 mols.) was treated in the cold with 0.4 gram of powdered sodium hydroxide. No rise of temperature was noticed, but after 8 hours' standing the solution had become faintly acid; 0.4 gram more of sodium hydroxide was then added and, after standing over night, the same treatment was continued daily for 4 days, using, therefore, in all 3.2 grams of sodium hydroxide. The solution was now again faintly acid and the presence of formaldehyde could still be detected by a faint odor; the water was removed by distillation (25 mm.), heating, finally, on a boiling water-bath for 0.5 hour; 41.4 grams of thick, yellowish oil—crude pentaerythrose—remained in the distilling flask. A portion of the oil, 18.4 grams, was dissolved in 65.2 grams of acetic anhydride and then heated for 8.5 hours at 100°. The acylated gum, left after distilling off the acetic acid and anhydride (25 mm.), heating finally in a bath at 100°, was found to weigh 32.7 grams. It was freed from 4.53 grams of insoluble sodium salts by dissolving in 400 cc. of warm ether. The ethereal filtrate was then washed with 160 cc. of 10 per cent potassium carbonate and dried with calcium chloride. The ether was distilled off and the last traces present removed by heating at 100° (20 mm.); 27 grams of a yellowish, mobile oil remained, which is evidently acylated pentaerythrose, containing also some acylated pentaerythrite and acetylated $\beta\beta'$ dihydroxyisobutyric aldehyde. The oil is insoluble or very sparingly soluble in water and all attempts to convert it into the solid state were fruitless. On distillation (30 mm.) 5.3 grams of the oil gave, with marked decomposition, 3.2 grams of distillate boiling at 215°–230°. Furthermore, the acylated oil, on treatment with phenylhydrazine, gave no well-defined derivative; the only thing left to do was to convert the oil back into pentaerythrose by hydrolysis with water. This was done by heating to 100° 3 times with 5

parts of water in periods of 10 hours each and distilling off the water and acetic acid after each operation under 20 mm., heating, finally, on a boiling water-bath. Twenty-nine and nine-tenths grams of acylated oil gave thus 17.8 grams, 16.1 grams and, finally, 15.5 grams of crude pentaerythrose as a highly viscous, yellowish oil. The oil is very soluble in cold water and alcohol, reduces Fehling's solution on warming, but all attempts to convert it into the solid state or into a crystalline derivative have, up to the present time, resulted in failure. That much pentaerythrose is present is proved, however, by the fact that the oil gives, on reduction with sodium amalgam in dilute acid solution,[1] a fair amount of pentaerythrite,[2] melting at 253°. For this purpose the crude pentaerythrose, obtained directly from the aqueous solution after condensation and subsequent removal of the water, was used; it contained, therefore, some sodium formate; 18.4 grams of gum were dissolved in 62.5 grams of water and treated, in the course of 6 hours, with 2.5 per cent sodium amalgam containing 9.3 grams of sodium, 1.5 times the theory, taking care to keep the solution at about 0° and faintly acid throughout the operation by continual addition of dilute sulphuric acid.

The water was then distilled off from the neutralized solution (20 mm.) and the salt residue, 67.5 grams, digested with 300 cc. of absolute alcohol, leaving 52.7 grams of insoluble salts. On cooling, the alcoholic filtrate gave 2.65 grams of pentaerythrite and on removing the alcohol entirely 9.6 grams of crystalline residue remained. The latter gave, on crystallization from a very small amount of water, 1.2 grams of a crystalline substance which melted at 170°–180°. The 12.25 grams of material soluble in the hot alcohol were finally resolved, by repeated fractional crystallization from water and alcohol, mainly into 2 products besides some unchanged pentaerythrose gum; namely, 3.2 grams melting at 220°–253°, from which 2.2 grams of practically pure pentaerythrite, m. p. 248°–253°, were obtained and 2.7 grams of substance melting between 170°–180°. It is extremely probable that this lower

[1] E. Fisher: Ber. d. chem. Ges., **23**, 3685.

[2] Tollens and Wigand: Ann. Chem. (Liebig), **265**, 322.

melting substance, which was also noticed by Tollens and Rave[1] in their work, is trihydroxytrimethylmethane,

$$(CH_2OH)_3 \vdots CH.$$

The analytical data given by Tollens and Rave, in fact, agree very well with those demanded by this compound. It must, therefore, be inferred that the crude pentaerythrose obtained in my experiments contains fairly large amounts of $\beta\beta'$ dihydroxyisobutyric aldehyde.

The following experiment with hydracrylic aldehyde and 2 mols. of formaldehyde proves that in this case also large amounts of pentaerythrose[2] are formed:

Nineteen and six-tenths grams of hydracrylic aldehyde, made according to Nef's directions,[3] but not distilled and simply freed from water and acrolein by heating in a bath at 80° (20 mm.), were dissolved in 78.4 grams of water; 45.4 grams of 35 per cent formaldehyde and, thereupon, 14 cc. of 1 per cent sodium hydroxide were added in the cold. A rise of 5° in temperature was noticed during the following 30 minutes and after 24 hours the solution had become neutral to litmus; 0.14 gram more of sodium hydroxide was now added daily for 13 days, or a total of 1.96 grams in all.

The aqueous solution, which was practically neutral and had still a faint odor of formaldehyde, was now freed from water by distillation (20 mm.), heating finally in a bath at 100° for 0.5 hour; 35 grams of crude pentaerythrose gum, containing some sodium formate, were thus obtained. The gum was dissolved in 107 grams of acetic anhydride[4] and heated at 100° for 9 hours; after getting rid of the acetic acid and anhydride by distillation (25 mm.) on a boiling water-bath, 58.9 grams of acylated gum were obtained. This was freed from 5.66 grams of sodium salts by dissolving in 300 cc. of warm ether. On distilling off the ether and removing the last traces by heating for 2 hours in a bath at 100° (18 mm.), 49.35 grams of a mobile, reddish

[1] Ann Chem (Liebig), **276**, 59, foot-note.

[2] Cf. Klüger: Monats. Chem., **26**, 885.

[3] Ann. Chem. (Liebig), **335**, 219.

[4] Special experiments with hydracrylic aldehyde and acetic anhydride have proved that at 100° no acetyl derivative but a non-volatile, at 300° (20 mm.), condensation product is formed.

acylated oil, insoluble in water, were obtained—obviously acylated pentaerythrose containing small amounts of acetylated pentaerythrite and $\beta\,\beta'$ dihydroxyisobutyl aldehyde.

Hydrolysis of the Acylated Oil.—The 49.35 grams of oil were now hydrolyzed by heating with 5 parts of water at 100°, for 10 hours, repeating the operation 3 times and removing the acetic acid, etc., formed by distillation (25–30 mm.) in a bath at 100°. The amount of non-volatile gum left after each treatment was 34 grams, 31.9 grams, and finally, 30.5 grams. The last portion obviously now consists mainly of pentaerythrose and shows a behavior which is in every way analogous to that shown by the crude pentaerythrose obtained from formaldehyde and acetaldehyde. It is a reddish, viscous gum, quite soluble in cold water and alcohol and reduces Fehling's solution on warming. Up to the present time all attempts to obtain a crystalline derivative, or to solidify the oil, have failed. The investigation of pentaerythrose will be continued in the near future. I wish especially to study also its oxidation products and to convert the crude pentaerythrose from hydracrylic aldehyde into pentaerythrite and trihydroxytrimethylmethane by means of sodium amalgam, in acid solution.

On the Action of Aqueous Copper Acetate on the Hexoses.

In view of the experimental difficulties presenting themselves in connection with the study of crude pentaerythrose and because of my desire to complete my studies during the present academic year, Dr. Nef suggested that I assist him in his study of the action of oxidizing agents on the sugars—a problem to which he has been devoting himself for over 2 years past.[1] The task assigned to me was the quantitative determination of the amount of cuprous oxide, carbon dioxide, formic, glycollic and oxalic acids formed from 100 grams of *d*-glucose, *d*-fructose and *d*-galactose by 8 hours' heating on a boiling water-bath with an excess, 10 mols., of aqueous copper acetate. Preliminary experiments by Nef, carried out in the autumn of 1904, had established the formation of the acids named except formic acid, and their relative amounts had also,

[1] Ann. Chem. (Liebig), **335**, 323–333.

in part, been ascertained by him. My own quantitative results confirm his observations in these particulars. The other acids formed in the oxidation with copper acetate, which give calcium salts very soluble in water and precipitated by alcohol and which constitute about 40 per cent of the total reaction products, are at present being investigated by Nef; it is obviously impossible to present a theory of the oxidation of hexoses until this work is completed.

d-Glucose and Copper Acetate.—Twenty grams of *d*-glucose, m. p. 140°–150°, dissolved in 50 grams of water, were added to a warm solution of 225 grams of crystallized copper acetate, $Cu(C_2H_3O_2)_2.H_2O$, 10 mols., in 2 liters of water. The mixture was heated for 8 hours on a boiling water-bath under a reversed condenser. This operation was repeated 5 times, and in all 99 grams of dextrose were taken. The amount of carbon dioxide given off with 10 grams of dextrose and a corresponding amount of aqueous copper acetate was determined in a special experiment, as follows: The mixture was heated for 8 hours on a boiling water-bath, during which period a steady stream of carbon dioxide-free air was passed through the solution and the gaseous products were drawn through 2 tall cylinders filled with saturated barium hydroxide solution; 5.46 grams of barium carbonate, well washed and dried at 100°, were obtained, which corresponds to 12.2 grams of carbon dioxide from 100 grams of dextrose. Nef obtained, in a similar experiment with 20 grams of dextrose, etc., after heating for 6 hours in an oil-bath at 100°–110°—at the higher temperature the reaction is more complete—13.2 grams of barium carbonate, corresponding to 14.75 grams of carbon dioxide from 100 grams of dextrose. It was noticed that most of the carbon dioxide, as well as the greater part of the cuprous oxide, is formed during the first hour's heating.

Nef obtained, in his experiment with 20 grams of dextrose, 64 grams of cuprous oxide, whereas the average amount obtained by me in 4 experiments was 59.6 grams for every 20 grams of *d*-glucose. It was proved by special experiments—by dissolving in hydrogen chloride, precipitating with hydrogen sulphide, etc.—that the cuprous oxide obtained was, in all

cases, practically free from cupric or cuprous oxalate. From these data the amount of oxygen taken up in the oxidation of *d*-glucose was 4.08 atoms in my experiments.

The aqueous filtrates from the cuprous oxide were now united, the copper still present in large amounts was precipitated by hydrogen sulphide and the filtrate freed from hydrogen sulphide by drawing air through the hot solutions under a reversed condenser. The water was then distilled off slowly under reduced pressure until the volume of the solution reached about 2 liters, whereupon small amounts of sulphuric acid, formed by the oxidation of the copper and hydrogen sulphides, were removed by digestion with small portions of barium hydroxide so that, finally, the solution contained traces of barium. The water in the aqueous filtrate was now removed by distillation (20 mm.) and to insure complete removal of the volatile fatty acids present the residual gum was again dissolved in water and the distillation, under reduced pressure, repeated, heating, finally, on a boiling water-bath for 0.5 hour.

As an end result, 99 grams of dextrose gave 63.5 grams of non-volatile gum and 17.185 liters of distillate, containing water, acetic and formic acids.

The amount of formic acid present in the distillate was determined quantitatively by H. C. Jones' method[1] with potassium permanganate—a method which depends upon the fact that acetic acid is not oxidized in sodium carbonate solution at 70°–80° with 0.1 N potassium permanganate, whereas, sodium formate, being relatively much dissociated according to

$$O : C\begin{matrix} H \\ ONa \end{matrix} \rightleftharpoons O : C< + NaO—H,$$

is oxidized quantitatively to carbon dioxide under these conditions.

Preliminary experiments with much acetic acid and known quantities of formic acid proved that the method is perfectly

[1] Am. Chem. Jour., **17**, 539. Cf. Lieben : Monats Chem., **14**, 146. Peau de St. Gilles: Ann. de chim. et d. Phys., (3), **55**, 388.

reliable; the results obtained, however, with the above-mentioned aqueous distillate are not absolutely final concerning the amount of formic acid present because the aqueous distillates, in the case of all hexoses used, were found to reduce Fehling's solution very slightly on vigorous boiling. This shows that some volatile sugar must be present, but I was unable to determine whether the product was formaldehyde or glycollic aldehyde; obviously, however, some of the permanganate must be used up in oxidizing this substance. Furthermore, it was ascertained by special experiment that the copper acetate used in all my work contained the following amount of reducible material: Copper acetate, 20 grams, were digested for 2 hours with 100 cc. of water, 100 cc. of saturated sodium carbonate solution and with 20 cc. of 10 per cent. sodium hydroxide and the solution was then filtered from the insoluble black copper oxide. The colorless filtrate was acidified and made up to 1 liter; 100 cc. of this solution were then made alkaline with sodium carbonate and treated with an excess of 0.1 N potassium permanganate at 70°–80°, for 0.5 hour; the solution was then acidified with sulphuric acid, treated with an excess of 0.1 N oxalic acid and titrated back with 0.1 N potassium permanganate. It was found thus that 12.52 cc. 0.1 N potassium permanganate are used up in oxidizing the impurities present in 20 grams of copper acetate; a corresponding correction, was, therefore, introduced, depending upon the amount of copper used in my oxidation experiments.

Thus the amount of formic acid present in the aqueous distillate, 17.185 liters, obtained from 99 grams of dextrose, was found to be 9.93 grams, as follows: One hundred cc. of the distillate were treated with sodium carbonate and an excess of 0.1 N potassium permanganate, at 70°–80°, for 0.5 hour; the solution was then acidified with dilute sulphuric acid, treated with an excess of 0.1 N oxalic acid and titrated back with 0.1 N potassium permanganate; 29.06 cc. of 0.1 N potassium permanganate were used up in this oxidation. Deducting the amount of permanganate necessary for the oxidation of the copper acetate used with 99 grams dextrose, we find that a total of 4317.6 cc. of 0.1 N potassium perman-

ganate is necessary for the oxidation of the formic acid. This corresponds, therefore, to 10.03 grams of formic acid for every 100 grams of dextrose taken.

Determination of the Oxalic and Glycollic Acid in the Non-volatile Gum.

The 63.5 grams of non-volatile acid gum obtained from dextrose was dissolved in hot water and digested for 2 hours with an excess, 64 grams, of powdered calcium carbonate. The 50.04 grams of insoluble calcium salts which were thus obtained were proved, by digestion with 100 cc. of water and 150 cc. of 30 per cent acetic acid, to consist of unchanged calcium carbonate and of 14.5 grams of calcium oxalate, corresponding to 8.9 grams of anhydrous oxalic acid.

0.2829 gram substance, dried at 100°–120°, gave, on ignition, 0.1081 gram CaO.

	Calculated for $CaC_2O_4.H_2O$.	Found.
Ca	27.45	27.29

The aqueous filtrate containing the soluble calcium salts and unchanged sugars was now concentrated, under reduced pressure, to a small volume and the calcium salts then precipitated by the addition of much alcohol. The salts which came down at first in a gummy state gradually get solid on rubbing with a pestle. The calcium salts still left in the aqueous alcoholic filtrate were then removed by further concentration and subsequent precipitation by alcohol. Thus a total of 46.8 grams of brown calcium salts was obtained. The quantity of calcium present, determined by ignition of a portion with sulphuric acid, was found to be 11.6 per cent. On dissolving the lime salts in a very small quantity of hot water a total of 5.57 grams of calcium glycollate, in 3 fractions, separated out on long standing. This corresponds to 3.25 grams of free glycollic acid and an analysis of the last 2 fractions, crystallized once more from water, gave the following result:

1.2161 grams substance, dried at 100°–120°, lost 0.3441 gram H_2O.

0.3086 gram of dry salt gave, on ignition, 0.0910 gram CaO.

	Calculated for $Ca(C_2H_3O_3)_2.4H_2O$.	Found.
H_2O	27.48	28.29
CaO	29.47	29.49

It is extremely probable that some calcium glycollate was still held in solution by the more soluble lime salts present, consequently my determinations of the amount of glycollic acid formed from the sugars are probably low both in the case of dextrose and of levulose.

On precipitating the lime in the aqueous filtrate from the 5.57 grams of calcium glycollate mentioned above, with the calculated amount of oxalic acid and then distilling off the water (20 mm.), heating, finally, in a bath up to 100°, 29 grams of gummy acids remained. These were converted, by digestion with 3 parts of acetic anhyhride at 100°, for 9 hours, etc., into 43.5 grams of acylated gum; only 26.2 grams of the gum dissolved on digestion with ether and the remainder, 17.3 grams of dark brown gum, gave, on threefold hydrolysis with 5 parts of water at 100°, 10.5 grams of dark brown acid tar.

The aqueous alcoholic filtrates obtained after the second precipitation of lime salts by alcohol were now concentrated to a small volume; it was proved by the addition of alcohol that only traces of lime salts are present. The amount of neutral, non-volatile gum present in the solution was, therefore, determined by distillation under reduced pressure, heating, finally, to 100°; 20.3 grams brown gum were thus obtained. It was shown, by titration with Fehling's solution, to contain 8.68 grams of dextrose, leaving, therefore, 11.62 grams of material undetermined. The presence of unchanged dextrose in the gum was established by the fact that a portion of the gum, when treated in the cold with aqueous phenylhydrazine acetate, gave a fair amount of the osazone of *d*-glucosone, m. p. 205°.

Finally, it should be mentioned that a special experiment with 9 grams of *d*-glucose and the corresponding amount of aqueous copper acetate was carried out in the usual manner, in which the absence of carbonic oxide, or of any other gaseous product except carbon dioxide, was established beyond a doubt.

Levulose and Copper Acetate.—One hundred grams of *d*-fructose, m. p. 102°–105°, were treated, in portions of 20 grams each, with aqueous copper acetate (10 mols.) for 8 hours in a boiling water-bath. The average amount of cuprous oxide obtained was 68.2 grams for every 20 grams of fruit sugar taken, whereas Nef obtained, in 1904, from a similar amount after 5.5 hours' heating in an oil- bath at 100°–110°, 71.5 grams of cuprous oxide. These results show that more oxygen is taken up in the burning of levulose than in that of dextrose. The difference must, however, be attributed in part to the fact that less unchanged sugar is found at the end of the experiment in the case of *d*-fructose, 2.9 per cent as compared with 8.8 per cent in the case of dextrose.

The amount of carbon dioxide formed was also found to be noticeably larger in this case, for 10 grams fruit sugar gave, on heating for 8 hours in a boiling water-bath with aqueous copper acetate, 7.25 grams of barium carbonate, which corresponds to 16.17 grams of carbon dioxide from 100 grams of levulose.

On removing the excess of copper in the combined filtrates from 100 grams of levulose by hydrogen sulphide, etc., 64.4 grams of non-volatile and very dark-colored gum remained in the distilling flask. This gave, on treatment with hot water, 10.25 grams of insoluble tar, and digestion of the aqueous filtrate with 80 grams powdered calcium carbonate, etc., gave 63.07 grams of insoluble calcium salts, which were proved to consist of unchanged calcium carbonate and of 10.65 grams of calcium oxalate, corresponding to 6.56 grams of anhydrous oxalic acid. The aqueous filtrate, containing the soluble calcium salts, gave, on concentration to about 100 cc. and after standing for 1 week, 7.68 grams of crude calcium glycollate; and this, on crystallization from 50 cc. of water, gave 3.4 grams of pure calcium glycollate in snow-white, bulky needles.

3.3817 grams substance, dried at 100°–120°, lost 0.917 gram H_2O.

0.2532 gram dried salt gave, on ignition, 0.0748 gram CaO.

	Calculated for $Ca(C_2H_3O_3)_2.4H_2O$.	Found.
H_2O	27.40	27.10
CaO	29.47	29.54

The aqueous filtrate from the 7.68 grams of crude calcium glycollate gave, on concentration and precipitation by alcohol, 48 grams of light-brown calcium salts which, on analysis, were found to contain 14.54 per cent of calcium; these gave, when digested with the calculated amount of oxalic acid, etc., 34.8 grams of non-volatile acid gums which were resolved by digestion with 500 cc. of ethyl acetate (6 times) and then with 5 parts of absolute alcohol (2 times) into 18.7 grams of gum soluble in ethyl acetate, 8.4 grams soluble in alcohol and 7.7 grams of dark-brown, tarry acid gum insoluble in these solvents.

In order to determine the amount of formic acid formed in the oxidation a duplicate experiment, carried out with 50 grams of levulose, gave the following result; the total aqueous distillate was found to require 3149.6 cc. of 0.1 N potassium permanganate for the oxidation of the formic acid, after making the usual corrections as stated above. From these data the amount of formic acid formed in the oxidation of 100 grams of levulose is found to be 14.50 grams. The non-volatile portion gave, on treatment with water, an excess of powdered calcium carbonate, etc., 4.89 grams of calcium oxalate, dried at 100°, corresponding to 3.01 grams of anhydrous oxalic acid.

0.3496 gram substance gave, on ignition, 0.1337 gram CaO.

	Calculated for $CaC_2O_4.H_2O$.	Found.
Ca	27.45	27.31

The aqueous filtrate containing the soluble calcium salts was concentrated to a small volume and the salts present precipitated by alcohol, in the usual manner. On digesting these with the calculated amount of oxalic acid, etc., 26.1 grams of brown, gummy acids were obtained. These gave, when digested successively with ethyl acetate and absolute alcohol, as above in the first levulose experiment, 12.5 grams of gum, soluble in ethyl acetate, 8.1 grams of gum soluble in alcohol and 5.5 grams of dark-brown insoluble acid tar.

On working up the aqueous alcoholic filtrates from the precipitated soluble calcium salts, by distillation under reduced pressure, heating, finally, in a bath at 100°, only 3.5 grams of

gum, practically free from calcium salts, were obtained; this was proved by titration with Fehling's solution, to contain 1.46 grams of unchanged levulose. Furthermore, an aqueous solution of the gum gave, on standing with aqueous phenylhydrazine acetate, the osazone of *d*-glucosone, m. p. 199°–202°. The experiment shows, therefore, that decidedly less unchanged sugar (2.9 per cent) remains in the case of levulose than in that of *d*-glucose (8.8 per cent) and *d*-galactose (8.5 per cent).

Copper Acetate and d-Galactose.—The amount of oxygen taken up and of carbon dioxide formed in the oxidation of *d*-galactose by aqueous copper acetate is noticeably less than in the case of fruit or grape sugar.

Fifty grams of *d*-galactose, m. p. 152°–154°, were treated in 3 portions with aqueous copper acetate, 8 hours, at 100°, in the usual manner. The average amount of cuprous oxide obtained fom 20 grams of *d*-galactose was only 55.3 grams and Nef obtained, in 2 experiments in 1904, an average of 58 grams on heating for 6 hours in an oil-bath at 100°–110°.

The amount of carbon dioxide obtained from 10 grams of *d*-galactose and the corresponding amount of aqueous copper acetate was only 0.463 gram (2.1 grams of barium carbonate) after 8 hours' heating on a boiling water-bath.

Titration of the aqueous distillate with potassium permanganate, in the usual manner, showed that a total of 2347.4 cc. of 0.1 N solution was necessary for the oxidation of the formic acid present. These data prove that 100 grams of *d*-galactose give 11 grams of formic acid. Forty-two and eight-tenths grams of non-volatile, gummy acids were obtained; these gave, on digestion with 40 grams of powdered calcium carbonate, etc., 36.2 grams of insoluble lime salts, containing, as shown by heating with dilute acetic acid, 9.38 grams of calcium oxalate, dried at 100°, and corresponding to 5.78 grams of anhydrous oxalic acid.

0.2321 gram substance gave, on ignition, 0.0892 gram CaO.

	Calculated for $CaC_2O_4.H_2O$.	Found.
Ca	27.45	27.45

In addition to this 0.72 gram of copper oxalate separated out from one galactose portion on standing, *i. e.*, before precipitating the copper in the filtrate from the cuprous oxide by hydrogen sulphide; therefore the amount of anhydrous oxalic acid obtained from 50 grams of *d*-galactose was 6.16 grams.

The aqueous filtrate from the insoluble calcium salts gave, on concentration and addition of alcohol, 29 grams of lime salts, dried at 80°–90°; these were found, by titration with Fehling's solution, to contain 1.19 grams of *d*-galactose, but the amount of calcium glycollate present was not determined in this case. Finally, the aqueous alcoholic filtrates from the precipitated lime salts were found, on distillation under reduced pressure, to contain 11.5 grams of gum; this material contained 3.06 grams of unchanged *d*-galactose, as determined by titration with Fehling's solution. Therefore, the total amount of unaffected galactose amounted to 4.25 grams or 8.5 per cent. The presence of this sugar was also established by treating a portion of the gum with aqueous phenylhydrazine acetate in the cold; on standing, a large amount of an osazone melting at 190° was obtained.

The Action of Aqueous Copper Acetate on Formaldehyde, Formic, Glycollic and Oxalic Acids.

The following experiments with aqueous copper acetate and the reagents named are of importance; first, they prove that the formic and carbonic acids obtained in the oxidation of the hexoses cannot possibly be attributed to the breaking down of a portion of the oxalic acid formed as an intermediate product; second, because they prove that the oxalic acid obtained cannot possibly come from an oxidation of glycollic acid; third, because they show, very decisively, that the carbon dioxide obtained from the hexoses cannot possibly come, to any appreciable extent, from an oxidation of formic acid:

(*a*) One hundred and twelve and five-tenths grams of copper acetate, dissolved in a liter of water containing 10 grams of formic acid (sp. gr. 1.22), were heated in a boiling water-bath for 6.5 hours under a reversed condenser. During the entire period a slow stream of air, free from carbon dioxide, was drawn steadily through the solution and then through 2 tall cylinders filled

with saturated barium hydroxide solution. A very small amount of carbon dioxide is slowly and steadily evolved, although no precipitation of cuprous oxide could be detected. Only 0.89 gram of barium carbonate, or 0.2 gram of carbon dioxide, was obtained.

(*b*) A similar experiment with 112.5 grams of copper acetate, 1 liter of water and 29 grams of 35 per cent formaldehyde gave, after heating in an air current for 6.5 hours on a boiling water-bath, no trace of barium carbonate, as shown by an absence of even turbidity in the cylinders containing the barium hydroxide.

(*c*) A mixture of 28 grams of copper acetate, 2 grams of glycollic acid, 2 grams of acetic acid and 1 liter of water was heated in a boiling water-bath for 6 hours in a manner entirely similar to (*a*) and (*b*), but no trace of cuprous oxide or carbon dioxide could be found.

(*d*) Two and five-tenths grams of crystallized oxalic acid, dissolved in water, were added to a warm solution of 28 grams of copper acetate, 25 grams of acetic acid and 900 grams of water. The oxalic acid is precipitated at once and completely as white cupric oxalate, and this is invariably the case, no matter what proportion of acetic acid is present. The mixture was now heated on a boiling water-bath for 8 hours under practically the same conditions as were employed in (*a*), (*b*) and (*c*); no change took place and no trace of carbon dioxide was evolved during this period.

This result is in marked contrast to that obtained with aqueous copper acetate and the 3 hexoses, where the oxalic acid found in the oxidation experiments remained entirely in the solution, *i. e.*, did not come down as cupric oxalate either with the cuprous oxide or subsequently from the filtrate which still contained much copper acetate even on long standing. It is, therefore, not improbable that the oxalic acid actually obtained from the hexoses, as stated above, may have been formed by the subsequent hydrolysis of an unknown intermediate product.

In conclusion, I wish to express a deep feeling of appreciation of the help and encouragement which Dr. Nef has given me in the whole course of this work.

SYRACUSE, N.Y.
PAT. JAN. 21, 1908